

COMBINED HORMONAL CONTRACEPTIVES (CHCs)

I. INTRODUCTION

Combined Hormonal Contraceptives contain both estrogen and progestin. The types of CHCs that are available include:

A. Combined oral contraceptives (COCs)

1. Most widely used reversible method of contraception in the United States. Low dose COCs offer high efficacy, safety, and convenience and provide a number of significant non-contraceptive health benefits.
2. COCs consisting of monophasic or multiphasic products (35 ug or less ethinyl estradiol and a low dose progestin) should be used.

B. Vaginal contraceptive ring (NuvaRing®)

1. Non-biodegradable, flexible and transparent vaginal ring made of ethylene vinyl acetate copolymers and magnesium stearate that is used for monthly combination hormonal contraception.
2. Contains two active components –
 - a. Ethinyl estradiol - an estrogen)
 - b. Etonogestrel - biologically active metabolite of desogestrel, a third generation progestin. Etonogestrel is also known as 3-keto-desogestrel.
3. When placed in the vagina each ring releases on average 120ug/day of etonogestrel and 15 ug/day of ethinyl estradiol over a three week period of use.

C. Transdermal contraceptive patch (Xulane®)

1. Combination transdermal contraceptive patch containing 6.0 mg norelgestromin (NGMN) and 0.75mg of ethinyl estradiol (EE).
2. The patch has a contact surface area of 20cm².
3. Releases 150 micrograms of norelgestromin and 20 micrograms of ethinyl estradiol into the bloodstream per 24 hours.
4. OrthoEvra® has been discontinued in the United States – now replaced by generic - Xulane®
5. The patch has a boxed warning that states the woman will be exposed to about 60% more estrogen than if you use typical birth control containing pill containing 35 micrograms of estrogen and that increased estrogen may increase risk of side effects including blood clots.
6. There are conflicting findings regarding increased risk of DVT.
7. Two recent studies (one comparing the patch to a pill with levonorgestrel and the other to a pill with norgestimate) found a two-fold increased risk of blood clots among women using the patch, although in absolute numbers, the risk remains very low. Even a two-fold increase risk is dwarfed by the risk of VTE associated with pregnancy.
8. A third study, recently updated with an additional 17 months of data, found no increase in risk for DVT in patch users compared to a norgestimate-containing pill. Clients need to be aware of this issue since there are ongoing lawsuits
9. . The FDA considers Xulane® safe and effective when it is used according to the labeling

II. CLIENT SELECTION

- A. Indications: CHCs may be provided when contraindications do not exist for contraception.
- B. Contraindications: USMEC 3-- Risks outweigh advantages for method use; USMEC 4-- Unacceptable risk for method use
 - 1. History deep vein thrombosis (DVT) or pulmonary embolism (PE) (USMEC 3)
 - 2. Current deep vein thrombosis (DVT)/pulmonary embolism (PE) (USMEC 3, 4)
 - 3. Major surgery with prolonged immobilization (USMEC 4)
 - 4. History of or current superficial venous thrombosis (USMEC 3)
 - 5. Stroke (history of cerebrovascular accident) (USMEC 4)
 - 6. Known thrombogenic mutations (e.g. Factor V Leiden, Prothrombin mutation, Lupus Anticoagulant, Protein C, Protein S and Antithrombin deficiencies) (USMEC 4)
 - 7. Smoking \geq 35 years of age
 - a. < 15 cigarettes/day (USMEC 3)
 - b. > 15 cigarettes/day (USMEC 4)
 - 8. History of or current ischemic heart disease (USMEC 4)
 - 9. Multiple cardiovascular risk factors (older age, smoking, diabetes, hypertension) (USMEC 3,4)
 - 10. Hypertension
 - a. Adequately controlled (USMEC 3)
 - b. Systolic \geq 160 or diastolic \geq 100 (USMEC 4);
 - c. Systolic \geq 140-159 or diastolic of 90-99 (USMEC 3)
 - d. Vascular disease (USMEC 4)
 - 11. Known hyperlipidemia (USMEC 2,3) (consult with medical director)
 - 12. Diabetes mellitus with nephropathy, retinopathy, neuropathy (USMEC 3,4)
 - 13. Other vascular disease or diabetes of > 20 years duration (USMEC 3,4)
 - 14. Medically diagnosed migraine with aura (USMEC 4)
 - 15. Multiple sclerosis with prolonged immobility (USMEC 3)
 - 16. Viral hepatitis (acute or flare) (USMEC 3,4)
 - 17. Cirrhosis-severe (decompensated) (USMEC 4)
 - 18. Solid organ transplant (complicated) (USMEC 4)
 - 19. Liver tumor (adenoma or hepatoma) (USMEC 4)
 - 20. Current breast cancer (USMEC 4)
 - 21. History of breast cancer and no evidence of disease for 5 years (USMEC 3)
 - 22. Valvular heart disease -complicated (pulmonary hypertension, history of sub-acute bacterial endocarditis, risk for atrial fibrillation) (USMEC 4)
 - 23. Peripartum cardiomyopathy (USMEC 3,4)
 - 24. Post-partum (non-breastfeeding or breastfeeding) < 21 days (USMEC 4)
 - 25. Post-partum (non-breastfeeding or breastfeeding) 21- 42 days with other risk factors for VTE (age \geq 35 years previous VTE, thrombophilia, immobility, transfusion at delivery, BMI 30 or >, post-partum hemorrhage, post cesarean delivery, preeclampsia, or smoker) (USMEC 3)
 - 26. Post-partum (breastfeeding) 21 - 30 days without VTE risk factors (USMEC 3)
 - 27. Gallbladder disease-- symptomatic (current or medically treated) (USMEC 3)

28. History of cholestasis- (past COC related) (USMEC 3)
29. Systemic Lupus Erythematosus – With positive (or unknown) antiphospholipid antibodies (USMEC 4)
30. Inflammatory bowel (ulcerative colitis, Crohns) (USMEC 2,3)
31. Bariatric surgery (history of)—malabsorption procedures (USMEC 3 for COC only)
32. Use of medications known to increase liver enzyme metabolism and thus may decrease contraceptive effectiveness. (USMEC 3):
 - a. **Anti Epilepsy Drugs (AEDs)** – may also be used to treat certain psychiatric illnesses, headaches, chronic pain and other conditions (USMEC 3):
 - i. Carbamazepine (Tegretol®)
 - ii. Oxcarbazepine (Trileptal®)
 - iii. Phenobarbital
 - iv. Phenytoin (Dilantin®)
 - v. Primidone (Mysoline®)
 - vi. Toprimate (Topamax®) – mild decrease
 - b. **Antiretroviral (ARV) therapy**
 - i. Fosamprenavir
 - c. **Anti-Mycobacterials**
 - i. Rifampin
 - ii. Rifampicin
 - iii. Rifamate

III. MANAGEMENT OF WOMEN WITH SPECIAL CONDITIONS REQUIRING FURTHER EVALUATION

- A. Decisions regarding individualized management, follow-up intervals, the need for additional testing or referral must be made based on protocols approved by the site Medical Director. In addition, there should be consultation with the site Medical Director if needed.
- B. *Request for Hormonal Contraceptives by Women with Risk Factors Consent Form* must be reviewed with client and signed and this must be documented in the medical record if medical conditions exist that are USMEC 3 or 4 (see above)
- C. Management of Medication Issues with Combined Hormonal Contraceptives
 1. ARVs - HIV positive women who choose to use hormonal contraception should be encouraged to use condoms with each act of intercourse. Choice of hormonal contraceptive should be based on the woman's ARV regimen and in consultation with the provider delivering HIV care.
 2. Anti-Epileptic Drugs (AEDS) and others listed above –use of monophasic is preferred. Use of back-up barrier methods and the benefits and risks of using DMPA, IUD, or sterilization as alternatives should be discussed with women who need a high degree of protection.
 3. Unlike popular belief, ost broad-spectrum antibiotics do not affect the contraceptive effectiveness of CHCs (USMEC 1).

IV. MEDICAL SCREENING AND EVALUATION

- A. There is no medical or safety benefit to requiring routine pelvic examination or cervical cytology before initiating hormonal contraception.
- B. A thorough history (with attention to determining presence of any medical conditions that would be a contraindication to CHC use), a review of systems (ROS) and basic physical that includes blood pressure, pulse, height and weight should be conducted prior to initiation of CHC.
- C. If indicated based on history, ROS or basic physical evaluation, a more detailed physical examination and/or laboratory testing may be indicated.
- D. Clients should be encouraged to have age appropriate routine physical exam, including pelvic exam and clinical breast exam as well as routine preventative services, but these are not a pre-requisite to the provision of CHC.

V. CLIENT EDUCATION/ INFORMED CONSENT

All clients being provided combined hormonal contraceptives should receive the following:

- A. Information/counseling regarding all contraceptive options available
- B. Information specific to combined hormonal contraceptive method of choice, including effectiveness, benefits, risks, use, danger signs, potential side effects, complications and discontinuation issues
- C. Instruction that contraceptive effectiveness may be reduced with co-administration of other drugs.
- D. Information that that CHCs provides no protection against STIs/HIV
- E. Method specific informed consent
- F. *Request for Hormonal Contraceptives by Women with Risk Factors Consent Form* must be signed by clients with special conditions/risk factors (such as diabetes, chronic hypertension, or multiple cardiovascular risk factors), as indicated.
- G. Instruction/counseling on importance of reading the Patient Package Insert (PPI)
- H. Written and verbal instruction on method use (may use Package Insert)
- I. Upon request, a copy of the method specific consent form
- J. Emergency, 24-hour telephone number and location where emergency services can be obtained
- K. Clinic access information

VI. PRESCRIBING COMBINED HORMONAL CONTRACEPTIVES

- A. Up to 14 cycles of CHCs may be prescribed for initial and annual clients
- B. Quick Start (same day start method) can be initiated if it is reasonably certain client is not pregnant and the client is not in need of emergency contraception.
 - 1. Instruct the client on the day of the clinic visit to:
 - a. Take the first pill in the pill pack, or
 - b. Insert the vaginal ring, or
 - c. Apply the first patch
 - 2. Instruct client to use a backup method (condoms, etc.) for 7 days.
 - 3. If there is concern about undetectable early pregnancy, the client should return for a repeat pregnancy test in 2 weeks. If the repeat pregnancy test is negative and the client has no signs of pregnancy (i.e. nausea, breast tenderness), continue the method.

4. The table below should be followed when initiating CHC. Alternative timings must be individualized to ensure contraceptive protection.

Timing of CHC Initiation

Current Method	CHC Initiation	Back-Up
No effective contraception	Anytime in cycle if it is reasonably certain client is not pregnant. If possibility of pregnancy is suspected, a highly sensitive urine test must be completed. If pregnancy test is negative, initiate COC and advise client to repeat urine test in 2 weeks.	If more than 5 days since menstrual bleeding started, back-up for 7 days
Correct use of vaginal contraceptive ring or transdermal contraceptive patch (changing to COC)	Within 24 hours of the removal of ring or patch	None
	At end of cycle, anytime within 7 days of last patch or ring removed.	None
Correct use of COC or patch (Changing to vaginal contraceptive ring)	Within 24 hours of the last COC tablet taken or patch removed	None
	At end of cycle, anytime within 7 days of last COC tablet or patch removed.	None
Correct use of COC or vaginal contraceptive ring (Changing to patch)	Anytime within 5 days of the last active COC tablet	None
	Within 24 hours of ring removal	None
Progestin-Only Pills (changing to COC)	Any day of the month. There should be no skipped days between last pill and first day of COC use.	None
Implant (changing to COC)	On same day implant is removed	Back-up method for 7 days
DMPA (changing to COC)	On day when next injection is due	None
Intrauterine contraception in place(changing to COC)	On same day IUD is removed	Back-up method for 7 days
Post-surgical abortion (starting to CHC)	Within five days of a completed procedure	None
Post-medical abortion (Can initiate prior to ultrasound confirmation)	Day of Misoprostol up to seven days after Mifepristone	None

of termination of pregnancy) (starting to CHC)	Beyond seven days after Mifepristone if intercourse not already resumed	Back-up method for 7 days
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- A. Clients should be provided an instruction sheet regarding management of deviations (e.g. missed pills, ring left in vagina >3 weeks) from the recommended CHC regimen

VII. MANAGEMENT OF SIDE EFFECTS AND COMPLICATIONS

- A. Warning Signs (ACHES) – May or may not be related to CHC use and further clinical evaluation is necessary to determine whether continuation of CHC is appropriate
- A—Abdominal pain
 - C—Chest pain
 - H—Headaches
 - E—Eye Problems
 - S—Severe Leg Pain
- B. Vaginal Bleeding - Irregular menstrual patterns (spotting to menstrual flow) are common in the first 2-3 cycles of use. If these patterns continue past the first three cycles or if heavy bleeding continues, the client needs to be assessed.
1. Irregular Bleeding – After determining consistent usage; no underlying pathology; R/O pregnancy; and if not at risk of STI's, reassure client. Use of a three-day course of NSAID's may help.
 2. Amenorrhea – rule out pregnancy
- C. Other side effects such as nausea, vomiting, breast tenderness, and headache should be further assessed to determine possible etiology and whether change in contraceptive method is needed.

VIII. FOLLOW-UP

- A. Clients should be provided an instruction sheet regarding management of deviations (e.g. missed pills, ring left in vagina >3 weeks) from the recommended CHC regimen
- B. A blood pressure check should be conducted within 3 weeks of initiation when woman is on active part of CHC (not when she is on placebo week or week off ring, patch, etc.). At this visit response to and satisfaction with method can be assessed.
- C. CHC user must be advised to return to the clinic for additional follow-up if:
1. A significant CHC related problem is suspected
 - a. She is at increased risk for complications resulting from CHC use
 2. Pre-hypertensive (SBP is 120-139 or DBP is 80-89) on two consecutive visits:
 - a. The client may continue CHCs but should be counseled regarding lifestyle modifications.
 - b. Referral to a primary care provider is also recommended.

- D. Please refer to Appendix A for management of clients on CHC who develop high blood pressure
- E. At each CHC related medical visit, the client should be queried about changes in personal history, headaches, blurred or double vision, pain or swelling in arms or legs, chest pain or shortness of breath, abdominal pain, jaundice, or severe depression.
- F. When starting a new method, especially with teens, can consider follow-up visit to check for adherence to method and to assess for method satisfaction.

IX. DOCUMENTATION

- A. Orders must be written in medical record initially, annually and upon method change.
- B. All CHCs distributed must be documented in the medical record and/or computer system.
- C. All education/counseling must be documented

REFERENCES

1. CDC Medical Eligibility Criteria for Contraceptive Use. MMWR, Vol. 57, No.RR-4, June 18, 2016.
2. ACOG. Committee Opinion. Access to Contraception. 2015.
3. ACOG. Guidelines for Women's Health Care: A Resource Manual, 4th Edition. 2014.
4. Hatcher RA et al. Contraceptive Technology. 20th Revised Edition. Ardent Media, Inc., New York, 2011.
5. Manufacturer's FDA Product Patient Insert

Appendix A

Management of Clients Using CHC Who Develop High Blood Pressure

Instruct client to return two or more times within a four week period for BP checks. At each visit, take two readings, five minutes apart, sitting in a chair. Confirm elevated readings in contralateral arm. Base decision on the average of these readings.

- A. If the average of at least two properly measured BPs at any visit is SBP ≥ 160 or DBP ≥ 100 :
 - 1. **Discontinue CHC.** (USMEC 4)
 - 2. Recommend or refer for medical evaluation
 - 3. Educate client on alternative methods of birth control.
 - 4. With client's consent, initiate a non-estrogen containing method. (Please note if prescribing DMPA, BP $\geq 160/100$ is a special condition requiring further evaluation)

- B. If the average of at least two properly measured BPs is SBP ≥ 140 -159 or DBP ≥ 90 -99 on at least two different visits:
 - 1. **Discontinue CHC** (USMEC 3)
 - 2. Educate client on alternative methods of birth control.
 - 3. With client's consent, initiate a non-estrogen containing method. (Please note if prescribing DMPA, BP $\geq 160/100$ is a special condition requiring further evaluation)
 - 4. Re-check BP within three months
 - 5. If BP returns to normal ($<120/80$) or pre-hypertensive range (SBP 120-139 or DBP 80-89), may consider initiating lower dose CHC, if available.

- C. If the average of two properly obtained readings each visit is SBP 120-139 or DBP 80-89 (prehypertension)
 - 1. May continue CHC
 - 2. Provide education on lifestyle modifications (dietary and exercise)
 - 3. Consider BP re-check in three to six months

- D. If $<120/80$ on all readings:
 - 1. May continue CHC.

(Source: NIH Publication No. 03-5231, 2003)